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EXAMINER	
AEDER, SEAN E	

ART UNIT	PAPER NUMBER
1642	

NOTIFICATION DATE	DELIVERY MODE
07/17/2007	ELECTRONIC

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Notice of the Office communication was sent electronically on above-indicated "Notification Date" to the following e-mail address(es):

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Office Action Summary	Application No.	Applicant(s)	
	10/516,946	PAU ET AL.	
	Examiner	Art Unit	
	Sean E. Aeder	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *07 May 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-13 and 17-25* is/are pending in the application.

4a) Of the above claim(s) *6,7,9,13 and 17-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-5,8,10-12,24 and 25* is/are rejected.

7)☒ Claim(s) *11* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Detailed Action

The Amendments and Remarks filed 5/7/07 in response to the Office Action of 11/6/06 are acknowledged and have been entered.

Claims 24-25 have been added by Applicant.

Claims 1-13 and 17-25 are pending.

Claims 6, 7, 9, 13, and 17-23 have been withdrawn.

Claims 1-5, 8, and 10-12 have been amended by Applicant.

Claims 1-5, 8, 10-12, 24, and 25 are currently under examination.

The following Office Action contains NEW GROUNDS of rejections necessitated by Amendments.

Objections Withdrawn

The objections to claims 4, 5, 8, and 10-12 are withdrawn.

Rejections Withdrawn

The rejection of claims 1-3 under 35 U.S.C. 112 second paragraph, for reciting "...characterized in that it involves the measurement of...", is withdrawn.

The rejection of claim 3 under 35 U.S.C. 112 second paragraph, for reciting "...in that it involves...", is withdrawn.

The rejection of claim 3 under 35 U.S.C. 112 second paragraph, because claim 2 recites "the cancer", is withdrawn due to the change in dependency of claim 3.

Response to Arguments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-3 remain rejected and claims 4, 5, 8, 10-12, 24, and 25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons stated in the Office Action of 11/6/06 and for the reasons set-forth below.

The Office Action of 11/6/06 indicates that claim 1 and dependent claims 2-3 are rejected for missing steps involving correlating specific results to a determination that a cell is or is not resistant to oxaliplatin treatment.

In response to the Office Action of 11/6/06, Applicant amended claim 1 to recite: "...wherein reduced expression of said effector or marker gene compared to a control cell not resistant to oxaliplatin indicates resistance to oxaliplatin".

The amendments found in the Reply of 5/7/07 have been carefully considered, but are not deemed persuasive. It is unclear *in what way* reduced expression of said effector or marker gene compared to a control cell not resistant to oxaliplatin "indicates" resistance to oxaliplatin. It is unclear whether said reduced expression "indicates" that a

cell is resistant to oxaliplatin because cells with reduced expression are oxaliplatin resistant or whether reduced expression "indicates" resistance to oxaliplatin wherein a cell is not resistant to oxaliplatin because cells with reduced expression are not oxaliplatin resistant. Amending claim 1 to recite: "...wherein reduced expression of said effector or marker gene compared to a control cell not resistant to oxaliplatin indicates ~~resistance to~~ **that said cancer cell is resistant to** oxaliplatin" would obviate this rejection.

Claim 2 remains rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention, for the reasons stated in the Office Action of 11/6/06 and for the reasons set-forth below.

The Office Action of 11/6/06 indicates that claim 2 lacks antecedent basis for the term "the cancer".

In response to the Office Action of 11/6/06, Applicant amended claim 2 to recite: "...The process of claim 1, wherein the cancer is...".

The amendments to the claims have been carefully considered, but are not deemed persuasive. While claim 1 recites "a cancer cell", claim 1 does not recite "a cancer". Therefore, claim 2 lacks sufficient antecedent basis for the term "the cancer". Amending "the cancer" in claim 2 to "the cancer cell" would obviate this rejection.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 3 remains rejected and claims 1, 2, 4, 5, 8, and 10-12 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement, for the reasons stated in the Office Action of 11/6/06 and for the reasons set-forth below.

The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. In the instant case, the claims are inclusive of: (1) a genus of mitochondrial apoptosis genes; (2) a genus of effector genes for mitochondrial apoptosis; (3) a genus of marker genes for mitochondrial apoptosis; and (4) a genus of apoptosis genes. The written description in this case sets forth Bax as a mitochondrial apoptosis gene (see page 12, in particular). The specification does not disclose, and the art does not teach, which other genes would or would not be encompassed by the genera. Neither the art not the specification indicate a particular structure shared by members of the genera.

A description of a genus may be achieved by means of a recitation of a representative number of species falling within the scope of the genus or by describing structural features common to that genus that "constitute a substantial portion of the genus." See University of California v. Eli Lilly and Co., 119 F.3d 1559, 1568, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997): "A description of a genus of cDNAs may be achieved by means of a recitation of a representative number of cDNA, defined by

nucleotide sequence, falling within the scope of the genus or of a recitation of structural features common to the members of the genus, which features constitute a substantial portion of the genus."

The inventions at issue in Lilly were DNA constructs per se, the holdings of that case is also applicable to claims such as those at issue here. Further, disclosure that does not adequately describe a product itself logically cannot adequately describe a method of using that product.

The court has since clarified that this standard applies to compounds other than cDNAs. See University of Rochester v. G.D. Searle & Co., Inc., F.3d, 2004 WL 260813, at *9 (Fed.Cir.Feb. 13, 2004). The instant specification fails to provide sufficient descriptive information, such as definitive structural or functional features that are common to the genus. That is, the specification provides neither a representative number of genes that encompass the genera nor does it provide a description of structural features that are common to the genera. Since the disclosure fails to describe common attributes or characteristics that identify members of the genera, and because the genera are highly variant, the disclosure of Bax is insufficient to describe the genera. Thus, one of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe and enable the genera as broadly claimed.

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession *of the invention*. The invention is, for purposes of the

'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See *Vas-Cath* at page 1116). The skilled artisan cannot envision the detailed chemical structure of the encompassed genera, and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method of isolation. The compound itself is required. See *Fiers v. Revel*, 25 USPQ2d 1601 at 1606 (CAFC 1993) and *Amgen Inc. v. Chugai Pharmaceutical Co. Ltd.*, 18 USPQ2d 1016.

One cannot describe what one has not conceived. See *Fiddes v. Baird*, 30 USPQ2d 1481 at 1483. In *Fiddes*, claims directed to mammalian FGF's were found to be unpatentable due to lack of written description for that broad class. The specification provided only the bovine sequence.

Applicant is reminded that *Vas-Cath* makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

In response to the Office Action of 11/6/06 Applicant amended claims.

The amendments to the claims have been carefully considered, but are not deemed persuasive for the reasons stated above.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3 remain rejected and claims 4, 5, and 8 are rejected under 35 U.S.C. 102(b), as being anticipated by Macpherson et al (Proceedings of the American Association for Cancer Research Annual meeting, 3/02, 43: 407-408), for the reasons stated in the Office Action of 11/6/06 and for the reasons set-forth below.

The Office Action of 11/6/06 contains the following text:

Macpherson et al teaches a process for in vitro detection of resistance of colorectal cancer cells to oxaliplatin treatment characterized in that it involves the measurement of mitochondrial apoptosis of cancer cells that are treated or can or are to be treated with oxaliplatin, further characterized in that it involves the measurement of the expression of Bax gene expression (see #2027 on pages 107-108, in particular).

It is further noted that Macpherson et al teaches a process for detecting the resistance of a colorectal cancer cell obtained from a patient to oxaliplatin treatment comprising detecting and measuring the expression of Bcl-xl by detecting mRNA transcripts of Bcl-xl, wherein reduced expression of Bcl-xl compared to a control cell not resistant to oxaliplatin indicates resistance to oxaliplatin (see abstract).

In response to the Office Action of 11/6/06, Applicant argues that Macpherson does not disclose an in vitro method of detection. Applicant argues that Macpherson

does not disclose the required step of measuring the expression of a mitochondrial apoptosis gene to detect the resistance of colorectal cancer cells to oxaliplatin treatment. Applicant further argues that Macpherson is directed to treatment for in vitro enhancement of the oxaliplatin cytotoxic effect and not a process of in vitro detection of such resistance.

The amendments to the claims and the arguments found in the Response of 5/7/07 have been carefully considered, but are not deemed persuasive. In response to the argument that Macpherson does not disclose an in vitro method of detection, Applicant is arguing a limitation not recited in the claims (in vitro detection). However, it is noted that Macpherson clearly teaches an in vitro detection method (see abstract). In regards to the argument that Macpherson does not disclose the required step of measuring the expression of a mitochondrial apoptosis gene to detect the resistance of colorectal cancer cells to oxaliplatin treatment, Macpherson teaches measuring the expression of Bcl-xl and correlating said expression to resistance of colorectal cancer cells to oxaliplatin treatment (see abstract). In regards to the argument that Macpherson is directed to treatment for in vitro enhancement of the oxaliplatin cytotoxic effect and not a process of in vitro detection of such resistance, Macpherson clearly teaches a process of in vitro detection of such resistance when correlating a decreased expression of Bcl-xl with oxaliplatin resistance (see abstract).

New Objections

Claim 11 is objected to because of an apparent typographical error. Claim 11 recites: "...using at least one primer for amplification of an mitochondrial apoptosis gene.". It is suspected Applicant may have intended claim 11 to recite: "...using at least one primer for amplification of ~~an~~ a mitochondrial apoptosis gene.". Proper correction is required.

New Rejections Necessitated by Amendments

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 24-25 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 24 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. Claim 24 recites a method "wherein reduced expression of mRNA encoding Bax compared to a control cell not resistant to oxaliplatin correlates with resistance to oxaliplatin"; however, 24 does not point-out *how* reduced expression of mRNA encoding Bax compared to a control cell not resistant to oxaliplatin correlates with resistance to oxaliplatin. It is unclear whether said reduced expression correlates with resistance to

oxaliplatin in a manner where a cell with reduced expression is resistant or whether a cell with reduced expression is not resistant. Thus, there is a missing step involving distinctly pointing-out *how* reduced expression of mRNA encoding Bax compared to a control cell not resistant to oxaliplatin correlates with resistance to oxaliplatin. See MPEP § 2172.01. It is further noted that possible limitations disclosed in the specification are not read into the claims.

Claim 25 is rejected under 35 U.S.C. 112, second paragraph, as being incomplete for omitting essential steps, such omission amounting to a gap between the steps. Claim 25 recites a method "wherein reduced expression of mRNA encoding Bak compared to a control cell not resistant to oxaliplatin correlates with resistance to oxaliplatin"; however, 24 does not point-out *how* reduced expression of mRNA encoding Bak compared to a control cell not resistant to oxaliplatin correlates with resistance to oxaliplatin. It is unclear whether said reduced expression correlates with resistance to oxaliplatin in a manner where a cell with reduced expression is resistant or whether a cell with reduced expression is not resistant. Thus, there is a missing step involving distinctly pointing-out *how* reduced expression of mRNA encoding Bak compared to a control cell not resistant to oxaliplatin correlates with resistance to oxaliplatin. See MPEP § 2172.01. It is further noted that possible limitations disclosed in the specification are not read into the claims.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a **NEW MATTER** rejection.

Claim 25 recites a method wherein reduced expression of mRNA encoding Bak compared to a control cells not resistant to oxaliplatin correlates with resistance to oxaliplatin. Descriptions of methods wherein reduced expression of mRNA encoding Bak compared to a control cells not resistant to oxaliplatin correlates with resistance to oxaliplatin are not found in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors, at the time the invention was filed, had possession of the claimed invention.

Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

Factors to be considered in determining whether undue experimentation is required, are summarized in *In re* Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). There are many factors to be considered when determining whether

there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any necessary experimentation is "undue." These factors include, but are not limited to: the breadth of the claims, the nature of the invention, the state of the prior art, the level of one of ordinary skill, the level of predictability in the art, the amount of direction provided by the inventor, the existence of working examples, and the quantity of experimentation needed to make or use the invention based on the content of the disclosure. See also *Ex parte* Forman, 230 USPQ 546 (BPAI 1986).

Claim 25 is drawn to a method wherein reduced expression of mRNA encoding Bak in a colorectal cancer cell compared to a control cell not resistant to oxaliplatin correlates with resistance to oxaliplatin.

The specification does not provide a written description for a method wherein reduced expression of mRNA encoding Bak in a colorectal cancer cell compared to a control cell not resistant to oxaliplatin correlates with resistance to oxaliplatin. Further, while the specification discloses Bak protein levels are elevated in response to oxaliplatin, changes in protein levels are not predictably indicative of changes in mRNA levels. In fact, the teachings of Greenbaum *et al.* (Genome Biology, 2003, Vol. 4, Issue 9, pages 117.1-117.8) cautions against assuming that mRNA levels are generally correlative of protein levels. The reference teaches (page 117.3, 2nd column) that primarily because of a limited ability to measure protein abundances, researchers have tried to find correlations between mRNA and the limited protein expression data, in the hope that they could determine protein abundance levels from the more copious and

technically easier mRNA experiments. To date, however, there have been only a handful of efforts to find correlations between mRNA and protein expression levels, most notably in human cancers and yeast cells. And, for the most part, they have reported only minimal and/or limited correlations. The reference further teaches (page 117.4, 2nd column) that there are presumably at least three reasons for the poor correlations generally reported in the literature between the level of mRNA and the level of protein, and these may not be mutually exclusive. First, there are many complicated and varied post-transcriptional mechanisms involved in turning mRNA into protein that are not yet sufficiently well defined to be able to compute protein concentrations from mRNA; second, proteins may differ substantially in their *in vivo* half lives; and/or third, there is a significant amount of error and noise in both protein and mRNA experiments that limit our ability to get a clear picture. The reference further notes (page 117.6, page 2nd column) that to be fully able to understand the relationship between mRNA and protein abundances, the dynamic processes involved in protein synthesis and degradation have to be better understood. Thus, the predictability of using mRNA levels as a diagnostic cannot predictably be determined by levels of protein expression due to the multitude of homeostatic factors affecting transcription and translation. Further, one of skill in the art would recognize that an increase in protein expression in response to a drug treatment does not predictably indicate that said protein is essential for efficacy of said drug treatment; rather, said increase in protein expression may likely be an inconsequential side-effect of said drug treatment.

The state of the prior art dictates that if expression levels of mRNA encoding Bak are to be used in a method of determining whether a cell is resistant to oxaliplatin, some resistance to oxaliplatin must be correlated with expression levels of mRNA encoding Bak. For example, Tockman et al (Cancer Res., 1992, 52:2711s-2718s) teach considerations necessary in bringing a cancer biomarker (intermediate end point marker) to successful application. Tockman et al teaches that prior to the successful application of newly described markers, research must validate the markers against acknowledged disease end points, establish quantitative criteria for marker presence/absence and confirm marker predictive value in prospective population trials (see abstract). Early stage markers of carcinogenesis have clear biological plausibility as markers of preclinical cancer and if validated (emphasis added) can be used for population screening (p. 2713s, col 1). The reference further teaches that once selected, the sensitivity and specificity of the biomarker must be validated to a known (histology/cytology-confirmed) cancer outcome. The essential element of the validation of an early detection marker is the ability to test the marker on clinical material obtained from subjects monitored in advance of clinical cancer and *link* those marker results with subsequent histological confirmation of disease. This irrefutable link between antecedent marker and subsequent acknowledged disease is the essence of a valid intermediate end point marker (p. 2714, see Biomarker Validation against Acknowledged Disease End Points). Clearly, prior to the successful application of newly described markers, markers must be validated against acknowledged disease end points and the marker predictive value must be confirmed in prospective population

trials (p. 2716s, col 2). While the teachings of Tockman are specifically addressing a diagnostic biomarker, the same principals are used in determining whether expression of a particular marker is predictably indicative of resistance to a particular therapeutic.

Further, it is noted that a publication *by Applicant* teaches a colon carcinoma model where modulation of Bak expression is *not* involved in acquisition of oxaliplatin resistance ((see right column of page 235 of Gourdier et al (FEBS Letters, October 2002, 529:232-236)).

Further, the level of unpredictability that just any maker is indicative of resistance to a particular drug is quite high. Since neither the specification nor the prior art provide evidence demonstrating that expression levels of Bak mRNA are indicative of resistance to oxaliplatin, a practitioner wishing to practice the claimed invention would be required to provide extensive experimentation to demonstrate such an association. Such experimentation would in itself be inventive.

In view of the teachings above and the lack of guidance, workable examples and or exemplification in the specification, it would require undue experimentation by one of skill in the art to determine with any predictability, that the method would function as claimed.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.

Claim 24 is rejected under 35 U.S.C. 102(a) as being anticipated by Gourdier et al (FEBS Letters, October 2002, 529:232-236).

Claim 24 recites a method wherein a colorectal cancer cell with reduced expression of mRNA encoding Bax compared to a control cell not resistant to oxaliplatin correlates with resistance to oxaliplatin.

Gourdier et al teaches a method wherein a colorectal cancer cell with reduced expression of mRNA encoding Bax compared to a control cell not resistant to oxaliplatin correlates with resistance to oxaliplatin (see page 233, and the "sequencing of the Bax gene", in particular).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was

not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-5, 8, and 10-12 are rejected under 35 U.S.C. 103(a) as being unpatentable over Macpherson et al (Proceedings of the American Association for Cancer Research Annual meeting, 3/02, 43: 407-408) as applied to claims 1-5 and 8 above, and further in view of Liu and Stein (Clinical Cancer Research, November 1997, 3:2039-2046).

Teaching of claims 1-5 and 8 by Macpherson et al is discussed above. Macpherson et al does not specifically teach precisely how Bcl-xl mRNA was detected. However, this deficiency is made up in the teachings of Liu and Stein.

Liu and Stein teaches a PCR method of detecting Bcl-xl mRNA levels by isolating mitochondrial DNA from a biological sample to be examined, or obtaining a cDNA from the RNA of the biological sample or from genomic DNA, and amplifying the DNA using at least one primer for amplification of Bcl-xl (right column of page 2040, in particular). Liu and Stein further teaches a process comprising contacting a nucleotide probe for Bcl-xl with a biological sample to be analyzed for a time and under suitable conditions for hybridization to occur, and detecting hybridization (right column of page 2040, in particular).

One of ordinary skill in the art at the time the invention was made would have been motivated to use the method taught by Liu and Stein to detect the Bcl-xl mRNA in the method taught by Macpherson et al because the method taught by Liu and Stein is

capable of measuring levels of Bcl-xl mRNA (page 2040, in particular). One of ordinary skill in the art at the time the invention was made would have had a reasonable expectation of success for performing the method taught by Liu and Stein to detect the Bcl-xl mRNA in the method taught by Macpherson et al because Liu and Stein teaches that Bcl-xl polynucleotides would be detected by said method (page 2040, in particular). Therefore, the invention as a whole would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made, absent unexpected results.

Summary

No claim is allowed.

Conclusion

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a). A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date

of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sean E. Aeder, Ph.D. whose telephone number is 571-272-8787. The examiner can normally be reached on M-F: 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shanon Foley can be reached on 571-272-0898. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SEA
/Misook Yu/
Primary Examiner, Art Unit 1642